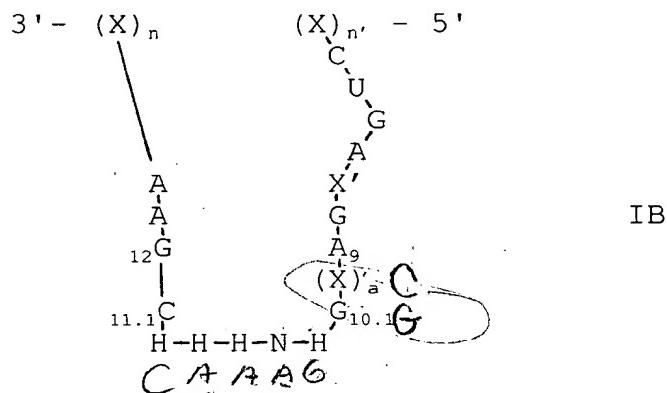
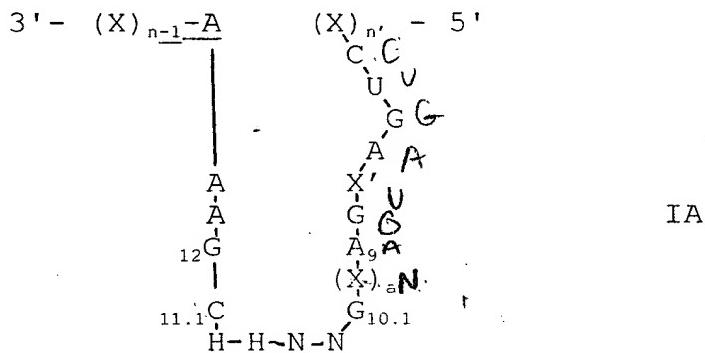


Applicants : Jason Francis Conaty et al.  
Serial No. : 09/887,880  
Filed : June 22, 2001  
Page 2

In the Claims

Please amend the claims pursuant to the provisions of proposed new rule 121 as described in the Official Gazette on February 25, 2003, as follows:

1. (Amended) A compound of the formula IA or IB:



wherein each X represents a nucleotide which may be the same or different and may be substituted or modified in its sugar, base or phosphate; and wherein  $G_{10.1}$  and  $C_{11.1}$  each represent a nucleotide which may be substituted or modified in its sugar (which may be ribose or deoxyribose), base or phosphate;

wherein each of C, G, A and U represents a ribonucleotide which may be substituted or modified in its sugar, base or phosphate;

wherein each of  $\underline{(X)_n}$   $\underline{(X)_{n-1}-A}$  and  $(X)_n'$  represents an oligonucleotide having a pre-determined sequence which is capable

Applicants : Jason Francis Conaty et al.  
Serial No. : 09/887,880  
Filed : June 22, 2001  
Page 3

~~ef~~ hybridizing hybridizes with an RNA target sequence to be cleaved, such RNA target sequence not being present within the compound, and each of n and n' represents an integer which defines the number of nucleotides in the oligonucleotide;

wherein X' represents a ribonucleotide selected from C, G, A and U which may be substituted or modified in its sugar, base or phosphate;

wherein a defines the number of nucleotides in  $(X)_a$  and may be 0 or 1 and if 0, the A located 5' of  $(X)_a$  is bonded to the G located 3' of  $(X)_a$ ;

wherein each solid line represents a chemical linkage providing covalent bonds between the nucleotides located on either side thereof;

wherein each N represents a nucleotide selected from C, G, A and U/T which may be substituted or modified in its sugar (which may be ribose or deoxyribose), base or phosphate and wherein each H represents a nucleotide selected from C, A and U/T, which may be substituted or modified in its sugar (which may be ribose or deoxyribose), base or phosphate; with the proviso that the sequence 5'-NNHH-3' is not UUUU or TTTT, CUCC, AAUU or GGCA.

- 61
2. (Amended) The compound of claim 1, wherein in the formula IB the oligonucleotide 3'-(X)<sub>n</sub>- is 3'-(X)<sub>n-1</sub>-A-.
  3. The compound of claim 1, wherein  $(X)_a$  is absent.
  4. The compound of claim 1, wherein the sum of n+n' is greater than 14.
  5. (Amended) The compound of claim 1, wherein the linker sequence 5'-NNHH-3' is a linker sequence selected from the following classes of linker sequences:

Applicants : Jason Francis Conaty et al.  
Serial No. : 09/887,880  
Filed : June 22, 2001  
Page 4

Class I: YRHH, wherein Y is C or U, R is G or A, and H is C, A or U;

Class II: DYHH, wherein D is G, A or U, Y is C or U, and H is C, A or U;

Class III: GHHA, wherein H is C, A or U; and

Class IV: WYHH, wherein W is A or U, Y is C or U, and H is C, A or U.

- b |
6. The compound of claim 5, wherein the linker sequence is selected from the sequences CGUU, UGUU and UAAC.
  7. The compound of claim 5, wherein the linker sequence is a sequence of the class WYHH, wherein W is A or U, Y is C or U, and H is C, A or U.
  8. The compound of claim 7, wherein the linker sequence is selected from the sequences ACCC, AUUU, UCCC, AUUC, AUUA, ACAC, AUAA and AUAC.
  9. The compound of claim 7, wherein the linker sequence is the sequence UUHH, wherein H is C, A or U.
  10. The compound of claim 9, wherein the linker sequence is selected from the sequences UUAC, UUCC, UUUC, UUUA, UUAA and UUAU.
  11. The compound of claim 5, wherein the linker sequence is selected from the sequences GUAA and GAUA.
  12. (Amended) The compound of claim 1, wherein the linker sequence 5'-HNHHH-3' in the compound of formula IB is selected from the sequences UCCCCA, UCCCC, UCCUA, AAUUU, UUAAA, UUUUA, UGUCC, UGUUA and CACCC.

Applicants : Jason Francis Conaty et al.  
Serial No. : 09/887,880  
Filed : June 22, 2001  
Page 5

13. (Amended) The compound of claim 12, wherein the linker sequence 5'-HNHHH-3' in the compound of formula IB is selected from the sequences UCCCC, UGUCC and CACCC.
14. The compound of claim 1, wherein each nucleotide in the linker sequence 5'-NNHH-3' or the linker sequence 5-HNHHH-3<sup>1</sup> is a deoxyribonucleotide.
15. A composition which comprises a compound of claim 1 in association with an acceptable carrier.
16. A composition which comprises a compound of claim 5 in association with an acceptable carrier.
17. An oligonucleotide transfer vector containing a nucleotide sequence which on transcription gives rise to the compound of claim 1 or claim 5.
18. The oligonucleotide transfer vector of claim 17, wherein the transfer vector is a bacterial plasmid, a bacteriophage DNA, a cosmid, or an eukaryotic viral DNA.
19. The oligonucleotide transfer vector of claim 17, wherein the oligonucleotide transfer vector is a plant DNA virus, a geminivirus or an infective phage particle.
20. The oligonucleotide transfer vector of claim 17, wherein the oligonucleotide transfer vector is packaged and contains the promoter sequences for RNA polymerase II or RNA polymerase III.
21. A host cell transformed by the transfer vector of claim 17.

/ isolated

Applicants : Jason Francis Conaty et al.  
Serial No. : 09/887,880  
Filed : June 22, 2001  
Page 6

22. The host cell of claim 21, wherein the host cell is a prokaryotic host cell or an eukaryotic host cell.
23. The prokaryotic host cell of claim 22, wherein the prokaryotic host cell is an *E.coli* host cell.
24. The eukaryotic host cell of claim 22, wherein the eukaryotic host cell is a monkey COS host cell, a Chinese hamster ovary host cell, a mammalian host cell or a plant host cell.
25. A method of cleaving a target mRNA in a subject which comprises administering to the subject an effective amount of the compound of claim 1 or claim 5.
26. The method of claim 25, wherein the administration is topical.
27. The method of claim 26, wherein the topically administered amount is between 1 ng and 10 mg.
28. The method of claim 25, wherein the administration is systemic.
29. The method of claim 28, wherein the systemically administered amount is between 1 ng and 500 µg/kg weight/day.
30. The method of claim 25, wherein the administration is by aerosol.
31. A method of cleaving a target mRNA in a host cell which

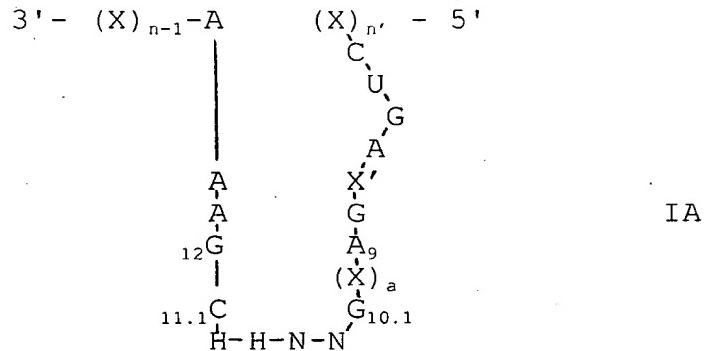
Applicants : Jason Francis Conaty et al.  
Serial No. : 09/887,880  
Filed : June 22, 2001  
Page 7

comprises administering to the host cell an effective amount of a compound of claim 1 or claim 5, or a transfer vector which on transcription expresses a compound of claim 1 or claim 5.

32. (Amended) The compound of claim 1 or claim 5 which further comprises an antisense nucleic acid which ~~is capable of hybridizing~~ hybridizes with an RNA target sequence.
33. (Amended) The compound of claim 1 or claim 5 which further comprises at least one additional non-naturally occurring oligonucleotide compound which comprises nucleotides whose sequence defines a conserved catalytic region and nucleotides whose sequence ~~is capable of hybridizing~~ hybridizes with a predetermined target sequence.
34. The compound of claim 33, wherein the additional non-naturally occurring oligonucleotide compound is a hammerhead ribozyme, a miniribozyme, a hairpin ribozyme, a hepatitis delta ribozyme, an RNAase P ribozyme, a Group I intron, or a combination thereof.

Applicants : Jason Francis Conaty et al.  
Serial No. : 09/887,880  
Filed : June 22, 2001  
Page 8

35. (New) The compound of claim 1 having the formula:



36. (New) The compound of claim 1 having the formula:

